

DOCKET NO.: ABI-0009



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#22
5/15/03
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Charles Vann et al.

Confirmation No.: **6464**

Serial No.: **09/506,870**

Group Art Unit: **1743**

Filing Date: **February 15, 2000**

Examiner: **Bex, Patricia K.**

For: **BEAD DISPENSING SYSTEM**

EXPRESS MAIL LABEL NO: EV160094609US
DATE OF DEPOSIT: May 8, 2003

Mail Stop Appeal-Brief Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPELLANTS' BRIEF PURSUANT TO 37 C.F.R. § 1.192

Applicants appeal the Final Rejection mailed October 9, 2002 in connection with the above-identified application.

I. Real Party in Interest

Based on information supplied by Applicants and to the best of the undersigned's knowledge, the real party in interest in the above-identified patent application is Applera Corporation, Applied Biosystems Group, of Foster City, California.

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II. Related Appeals and Interferences

There are no other appeals or interferences known to Appellants, Appellants' legal representative, or the assignee that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending Appeal.

III. Status of Claims

Claims 1-25 and 48-62 are pending in this patent application and are the subject of this Appeal. Claims 1-25 and 48-62 stand rejected. The Examiner has indicated that dependent claims 53 and 56 would be allowed if rewritten to include all of the limitations of the base claim and any intervening claims. Claims 1-25 and 48-62 appear in Appendix A.

IV. Status of Amendments

Claims 21-24, 51, and 54-57 have been amended since the issuance of the Final Rejection. The amendment was considered and entered (See Advisory Action mailed January 29, 2003).

V. Summary of the Invention

The present invention is directed to a system for picking up a plurality of beads from a supply and transferring them to a desired location (Specification, page 3, lines 2-4). The beads are capable of carrying substances such as reagents or samples (Specification, page 1, lines 8-9). The system includes an array of projections 54a-54l on a support 58a-58b (Specification, page 19, lines 15-17 and FIG. 1). The projections have cavities 70 with a lower opening to pick up the beads. (Specification, page 14, lines 13-15, and FIG 4A). The beads are drawn into the cavities and releasably retained within the cavities with an attraction force (Specification, page 14, lines 15-18). While retained in the cavities, the beads can be moved from one place to another with movement of the support (Specification, page 14, lines 18-19).

In addition to the lower opening, the cavities also have sidewalls 76 and an upper ceiling region 74 to help contain the beads (Specification, page 14, lines 13-15, and FIG 4A).

The composite of the cavity elements is generally that of an inverted cup-like structure (Specification, page 20, lines 28-29). In preferred embodiments, the cavity can receive one entire bead (Specification, page 21, lines 5-9).

VI. Issues

This appeal seeks to resolve eight issues:

1. whether claims 1, 3, 6, 7, and 14-17 are unpatentable under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,685,480;
2. whether claims 2, 4, 5, 8, 9, and 11-18 are unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of U.S. Patent No. 4,685,480, and Japanese Publication 80862 or U.S. Patent no. 4,937,048;
3. whether claim 10 is unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of U.S. Patent No. 4,685,480, U.S. Patent no. 4,937,048, and U.S. Patent No. 5,272,510;
4. whether claims 19, 20, and 48-50 are unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of U.S. Patent No. 4,685,480, U.S. Patent no. 4,937,048, and PCT Publication WO 97/38318;
5. whether claims 21-25, 55, 57-59 are unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of U.S. Patent No. 4,685,480, U.S. Patent no. 4,937,048, and U.S. Patent No. 6,288,220;
6. whether claims 21-24, 51, 54, and 57-59 are unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of U.S. Patent No. 4,685,480, U.S. Patent no. 4,937,048, and EPO Publication EP0955084;
7. whether claims 21 and 52 are unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of U.S. Patent No. 4,685,480, U.S. Patent no. 4,937,048, and U.S. Patent No. 4,236,825; and
8. whether claims 60-62 are unpatentable under 35 U.S.C. § 103(a) as being obvious over the combination of U.S. Patent No. 4,685,480, U.S. Patent no. 4,937,048, and U.S. Patent No. 5,447,736.

VII. Grouping of the Claims

Applicants grouping of claims is for purposes of this appeal only. As set forth in Applicants' request for reconsideration of the final rejection as premature in Applicants'

amendment filed January 8, 2003, a clear issue between the Applicants and the Examiner has not been developed. Accordingly, Applicants could present most, if not all, of the pending claims as an independent group for a total of about forty claim groupings. But to simplify the issues and for purposes of this appeal only, Applicants have attempted to minimize the number of claim groupings and do not advance additional claim groupings at this time. Accordingly, Applicants group the claims for purposes of this appeal in twenty-two groups as follows:

Claims 1 and 6 stand or fall together, independently of other claims.

Claims 2, 12, and 13 stand or fall together, independently of other claims.

Claims 4, 5, and 18 stand or fall together, independently of other claims.

Claims 8 and 9 stand or fall together, independently of other claims.

Claims 15 and 17 stand or fall together, independently of other claims.

Claims 19, 20, and 48-50 stand or fall together, independently of other claims.

Claims 22-24, and 57-59 stand or fall together, independently of other claims.

Claims 60-62 stand or fall together, independently of other claims.

Claims 3, 7, 10, 11, 14, 16, 21, 25, 51, 52, 53, 54, 55, and 56 each stand or fall alone, independently of other claims.

VIII. Arguments

1. The rejection of claims 1, 3, 6, 7, and 14-17 under 35 U.S.C. § 102(b) as allegedly being anticipated by Eck is improper

A) Claims 1, 6, 15, and 17

The rejection of claims 1, 6, 15, and 17 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,685,480 (the "Eck patent") is improper because the Eck patent does not disclose features recited in the rejected claims, including a system for picking up and transferring a plurality of beads, a cavity formed with an upper ceiling region and a sidewall, and an attraction source effective to draw beads from a bead supply and releasably retain the beads therein.

The Eck patent discloses a combined washer and aspirator that reduces the amount of manual dexterity required of a laboratory technologist to wash beads in reaction wells that are used in diagnostic immunoassays. As disclosed by the Eck patent, the lower portions of the inner tubular members 22 comprise tips 46 which mate with the reaction well seals 42, tip

seals 34, and outer tubular members 20. As best shown in FIGS. 3 and 4, each tip 46 has tip grooves 48, a cylindrical portion 50, a skirt 52, positioning means 54, deflecting means 56, a recessed portion 58, and protrusions 60 (Eck at column 2, lines 45-51).

The protrusions 60 of tip 46 of the Eck device act to hold beads 72 in a spaced manner away from the tips 46 to allow a flow of wash solution around the beads 72, thereby allowing the wells 68 and the beads 72 to be washed in place without removing the beads from the wells of the reaction tray. Protrusions 60 are required in the wash and aspiration device disclosed by the Eck patent in order for the device to work properly as a wash and aspiration device. Protrusions 60 prevent the beads from fully entering the tip 46 and help to maintain a fluid passageway between the tip and the bead.

The device disclosed by the Eck patent is for washing the wells 68 of a reaction tray 70 and beads 72 contained within the reaction tray 70 and is not for picking up the beads from the individual wells of the reaction tray; nor is the device disclosed by the Eck patent for transferring the beads from the reaction trays to another desired location. A technologist initiates a wash cycle by placing the wash and aspiration device 10 over a reaction tray 70 and then activating a flow of wash solution into parallel fluid passage 12, while at the same time, parallel passage 14 and inner concentric fluid passage 18 are connected to a vacuum source for the aspiration of the fluid wash solution out of the well 68 of the reaction tray 70. Significantly, the Eck patent does not disclose an apparatus for picking up a plurality of submillimeter beads from a bead supply and transferring the beads to a desired location.

correct
intended
use
in preamble

The Examiner states that the Eck device "is capable of" transferring beads to a desired location (January 29, 2003 Advisory Action page 2). Assuming, *arguendo*, the inherent design of the Eck device allows it to be used to transfer beads, this "odd use" of the Eck device is insufficient to establish anticipation.¹ Inherency may not be established by probability or possibilities. *In re Robertson*, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999). In *Robertson*, the Board found applicant's claim directed to a third fastener for a closing a diaper for disposal purposes anticipated because the diaper fastening means of a prior art reference was "capable of" operating as a third fastener to close the diaper for disposal. The Federal Circuit reversed the Board's finding of invalidity stating the Board's analysis rested

¹ Applicants do not agree that the Eck device is capable of transferring beads, but to simplify the issues and for purposes of this appeal only, Applicants do not advance that additional argument here.

upon "the very kind of probability or possibility – the odd use of fasteners with other than their mates" - that the court has pointed out is insufficient to establish inherency. *Id.*

Undoubtedly, the use of the Eck device as a means for transferring beads would be an odd use for the washer and aspirator. A central purpose of the Eck device is to wash beads "in reaction wells" (Eck column 1, lines 7-10). There is no need to transfer the beads after they have been washed and aspirated in the reaction wells (See Eck, column 1, lines 11-30). Accordingly, the Eck patent does not disclose or teach *a system for picking up a plurality of submillimeter beads from a bead supply and transferring the beads to a desired location*, as recited in claims 1, 6, 15, and 17 of the present application.²

Intended use limitation is preemptive

Further, the Eck patent does not disclose or teach *a cavity formed at a lower end region of each of said projections, each of said cavities defined by (i) a lower opening, (ii) an upper ceiling region, and (iii) a sidewall extending between said lower opening and said upper ceiling region; wherein said upper ceiling region defines a surface extending inwardly from said sidewall*, as recited in claims 1, 6, 15, and 17 of the present application. The cavity in the Eck device has a single surface having a radius.³ In the Final Rejection, on page 3, the Examiner presented FIG. 3 of the Eck patent with indications of the alleged inwardly sloped upper ceiling region and downwardly extending sidewall. The downwardly extending sidewall indicated by the Examiner on tip 46, however, is also the upper ceiling identified by the Examiner.⁴ Applicants' claims recite *cavities defined by... an upper ceiling region and a sidewall*. The Eck patent does not disclose a device having *cavities defined by... an upper ceiling region and a sidewall* as recited in Applicants' claims.

also appears to be the same surface in applicants' Fig 4A 4B continuous surface

claim does not exclude the ceiling & walls from being formed of same surface

² In the January 29, 2003 Advisory Action, the Examiner alleges that the recited language should not be considered as a limitation because it appears in the preamble of the claim. The preamble of claim 1 recites "picking up a plurality of submillimeter beads from a bead supply and transferring them to a desired location." The body of claim 1 then recites "an attraction source ... to draw beads from said supply." (Emphasis added). By referring to "said supply," the body of the claim expressly incorporates limitations in the preamble. See, e.g., *Electro Sci. Indus., Inc. v. Dynamic Details, Inc.*, 64 USPQ2d 1781, 1783 (Fed. Cir. 2002) (finding preamble limited the claim because the body of the claim relied upon and derived antecedent basis from the claim's preamble); *Bell Communications Research, Inc. v. Vitalink Communications Corp.*, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995) (finding the phrase "said packet" appearing in the claim body expressly incorporated by reference the preamble phrase "said packet including a source address and a destination address").

Applicant is correct

- No desired location in body of claim

³ The cavity surface of the Eck device tip 46 also includes protrusions 60 not relevant to this analysis.

⁴ The sidewall identified by the Examiner cannot be the outside surface of the tip 46 as the Examiner's arrow indicates because Applicants' claims recite that the sidewall defines the cavity.

↓

Further, the Eck patent does not disclose or teach *an attraction source, operable at said projection end regions, effective to draw beads from said supply into said cavities and to releasably retain said beads therein*, as recited in the claims of the present application. The only attraction source disclosed in the Eck patent is a vacuum used to remove and aspirate the wash solution from the reaction wells (Column 3, lines 22-50). Accordingly, the Eck patent does not disclose *an attraction source, operable at said projection end regions, effective to draw beads from said supply into said cavities and to releasably retain said beads therein* as recited in Applicants' claims.

Thus, the rejection of claims 1, 6, 15, and 17 under 35 U.S.C. § 102(b) as being anticipated the Eck patent is improper because the Eck patent does not disclose features recited in the rejected claims, including a system for picking up and transferring beads, a cavity formed with an upper ceiling region and a sidewall, and an attraction source effective to draw beads from a bead supply and releasably retain the beads therein. Withdrawal of the rejection of claims 1, 6, 15, and 17 under 35 U.S.C. § 102(b) is respectfully requested.

B) Claim 3

The rejection of claim 3 under 35 U.S.C. § 102(b) as being anticipated by the Eck patent is improper for all of the reasons that claim 1 is not anticipated because claim 3 depends from claim 1. In addition, with respect to claim 3, the Eck patent does not disclose or teach a cavity having *a substantially constant diameter sidewall along a region extending between its lower opening and its upper ceiling region, such that lines extending longitudinally along confronting inner surfaces of each sidewall are substantially parallel to one another*, as recited in claim 3. The cavity of tip 46 in the Eck patent has a radial surface that does not have *a substantially constant diameter* as recited in claim 3. For this additional reason, withdrawal of the rejection of claim 3 is requested.

what is acceptable degrees of freedom for term substantially?

C) Claim 7

The rejection of claim 7 under 35 U.S.C. § 102(b) as being anticipated by the Eck patent is improper for all of the reasons that claim 1 is not anticipated because claim 7 depends from claim 1. In addition, with respect to claim 7, the Eck patent does not disclose or teach *a plurality of ampules for containing a bead supply* as recited in claim 7. As

Eck has 70 ampules 65

discussed above, the Eck patent does not disclose an apparatus for picking up a plurality of submillimeter beads from a bead supply and transferring the beads to a desired location. Accordingly, the Eck patent does not disclose *a plurality of ampules for containing a bead supply*. For this additional reason, withdrawal of the rejection of claim 7 is requested.

D) Claim 14

The rejection of claim 14 under 35 U.S.C. § 102(b) as being anticipated by the Eck patent is improper for all of the reasons that claim 1 is not anticipated because claim 14 depends from claim 1. In addition, with respect to claim 14, the Eck patent does not disclose or teach *a cavity formed by a resiliently flexible, tubular sleeve fit over the end of a respective projection*, as recited in claim 14. In the Final Rejection on page 4, second paragraph, the Examiner admits that Eck does not "specifically recite the sidewall of each projection comprising a resiliently flexible material." For this additional reason, withdrawal of the rejection of claim 14 is requested. Tip 46
sheave
type of material
not
stated.

E) Claim 16

The rejection of claim 16 under 35 U.S.C. § 102(b) as being anticipated by the Eck patent is improper for all of the reasons that claim 1 is not anticipated because claim 16 depends from claim 1. In addition, with respect to claim 16, Eck does not disclose or teach *a system wherein each of the pressure-control assembly includes . . . a pump operable to establish an increased pressure within each of said lumens, said increased pressure effective to displace any beads retained in the cavities*, as recited in claim 16. Although Eck discloses a pressure source 12 for feeding wash solution into the tip 46, the pressure source is in fluid communication through channels 62, 64, and 66 with the **lower opening** of the tip. The fluid path then continues to fluid passage 18. Thus, any pressure created in the fluid passage 18 by the pressure source 12 will be less than the pressure created at the lower opening of the tip. Accordingly, the pressure source 12 cannot act to displace a bead retained in the tip. Thus, the Eck patent does not disclose an *increased pressure effective to displace any beads retained in the cavities*, as recited in claim 16. For this additional reason, withdrawal of the rejection of claim 16 is requested. ?

2. The rejection of claims 2, 4, 5, 8, 9, and 11-18 under 35 U.S.C. § 103(a) as allegedly being obvious over Eck in view of Ikeda or Sakai is improper

A) Claims 2, 12, and 13

The rejection of claims 2, 12 and 13 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view of Japanese publication JP 64-80862 (the "Ikeda reference") or U.S. Patent No. 4,937,048 (the "Sakai patent"), is improper because the cited references do not disclose a sidewall with a lower portion comprising *a resiliently flexible material, such that said flexible lower portion of said sidewall can bend while maintaining the shape of said cavity so that said lower opening can bend to face said beads in said bead supply*, as recited in the claims.

Eck is described in detail above. As discussed above, the Eck patent fails to disclose all of the features recited in the claims, including a resiliently flexible sidewall.

The Ikeda reference does not cure the deficiencies of the Eck patent. The Ikeda reference discloses a method for moving a spherical carrier (i.e. bead). The method taught by the Ikeda reference functions to prevent contamination from a cleaning liquid that co-exists with the bead by striking the bead against a sidewall of a vessel and dislodging the carrier while maintaining a vacuum. The cleaning fluid remaining in the nozzle is prevented from dropping because of the vacuum.

The Ikeda reference discloses several embodiments, including several embodiments that do not include a cavity formed at a lower end region of the projection (see FIGS. 1, 2, 3, 4(2), 4(3), and 5) and one embodiment that has a flared tip 2a on nozzle 2. However, the flared tip 2a of the Ikeda reference does not include a sidewall that *comprises a resiliently flexible material*, as recited in claims 2, 12, and 13.

The Sakai patent does not cure the deficiencies of the Eck patent and Ikeda reference. The Sakai patent discloses a carrier transporting apparatus and carrier container for use in an immunological analysis. In one embodiment, shown and described with reference to FIG. 13, the carrier transporting apparatus comprises a hopper 213 for holding a number of carriers 212. A suction nozzle 218 having an elastic mouth portion 217 is arranged movably between the carrier suction position in the carrier container 211. The suction nozzle 218 is moved to the carrier suction position through the vertical duct 215, so that the elastic mouth portion 217 is brought into contact with the carrier 212. As shown in FIG. 13, paying particular attention to the placement of the elastic mouth portion 217 identification leader, the elastic mouth

portion includes the entire fixture connected to the suction nozzle 218. An examination of FIG. 13, shows that it is the suction nozzle 218 that may bend and cause the cavity to face the beads in the bead supply, not the lower portion of a sidewall. Accordingly, the Sakai patent does not disclose a *flexible lower portion of a sidewall that can bend while maintaining the shape of the cavity so that said lower opening can bend to face the beads in the bead supply*, as recited in the claims.

Thus, the rejection of claims 2, 12, and 13 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view the Ikeda reference or the Sakai patent is improper because the cited reference do not disclose a sidewall with a lower portion comprising a *resiliently flexible material, such that said flexible lower portion of said sidewall can bend while maintaining the shape of said cavity so that said lower opening can bend to face said beads in said bead supply*, as recited in the claims. Withdrawal of the rejection of claims 2, 12, and 13 under 35 U.S.C. § 103(a) is respectfully requested.

B) Claims 4, 5, 15, 17, and 18

The rejection of claims 4, 5, 15, 17, and 18 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view the Ikeda reference or the Sakai patent is improper because the cited reference do not disclose all of the features recited in the claims. As discussed above, the Eck patent does not disclose features recited in the rejected claims, including a system for picking up and transferring a plurality of beads, a cavity formed with an upper ceiling region and a sidewall, and an attraction source effective to draw beads from a bead supply and releasably retain the beads therein.

In the Final Rejection, the Examiner asserts, without explanation, that the Sakai patent discloses the claimed invention except for the dimensions of the cavity (page 5, lines 3-4). The Sakai patent, however, fails to disclose other features recited in the rejected claims including a system for picking up and transferring a plurality of beads and a cavity formed with an upper ceiling region and a sidewall. Likewise, the Ikeda reference fails to disclose features recited in the rejected claims including, *inter alia*, a cavity formed with an upper ceiling region and a sidewall. As discussed above, the Eck patent also fails to disclose these features. Thus, the rejection is improper.

The rejection for alleged obviousness is also improper because the Examiner has failed to identify any teaching in the cited references that would have motivated modifying

the prior art in a way that would have lead to a claimed invention. Patent claims cannot be found obvious in view of a combination of references unless the prior art itself suggests the desirability of the combination. *Berghauser v. Dann*, 204 U.S.P.Q. 393 (D.D.C. 1979); *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 221 U.S.P.Q. 929 (Fed. Cir. 1984). To establish a *prima facie* case of obviousness, “there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant.” *In re Dance*, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998). “In other words, the examiner must show reasons that the skilled artisan, confronted with the same problem as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.” *In re Rouffet*, 47 USPQ2d 1453, 1458 (Fed. Cir. 1998).

Significantly, however, the Examiner does not identify any reason why the skilled artisan would have been motivated to combine the respective teachings of the cited references in a way that would have produced a claimed invention. Although the Examiner asserts that it would have been obvious to one of ordinary skill in the art to combine the teachings of the cited references, the Examiner does not appear to take account of the fact that the references are directed to different fields of endeavor. The Eck patent, for example, is directed to washing and aspirating beads, whereas the Sakai and Ikeda references are directed to transporting beads. There are substantial differences in the design and operating parameters one would consider for an apparatus to wash beads as compared to an apparatus to transport beads.

Thus, the rejection of claims 4, 5, 15, 17, and 18 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view the Ikeda reference or the Sakai patent is improper because the cited reference do not disclose all of the features recited in the claims. Further, the rejection is improper because the Examiner has not provided any evidence to combine the references. Accordingly, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

C) Claims 8 and 9

The rejection of claims 8 and 9 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view the Ikeda reference or the Sakai patent is improper for all of the reasons that claims 4, 5, 15, 17, and 18 are not obvious. In addition, with respect to claims 8

and 9, the cited references fail to teach or disclose *a plurality of covers, each cover configured to extend over an upper opening of one of said ampules*, as recited in the claims. For this additional reason, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

D) Claim 11

The rejection of claim 11 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view the Ikeda reference or the Sakai patent is improper for all of the reasons that claims 4, 5, 15, 17, and 18 are not obvious. In addition, with respect to claim 11, the cited references fail to teach or disclose *a plurality of ampules with a first and second reagent sets that differ from each other by at least one analyte-specific component*, as recited in claim 11. For this additional reason, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

E) Claim 14

The rejection of claim 14 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view the Ikeda reference or the Sakai patent is improper for all of the reasons that claims 4, 5, 15, 17, and 18 are not obvious. In addition, with respect to claim 14, the cited references fail to teach or disclose *a cavity formed by a resiliently flexible, tubular sleeve fit over the end of a respective projection*, as recited in claim 14. For this additional reason, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

F) Claim 16

The rejection of claim 16 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view the Ikeda reference or the Sakai patent is improper for all of the reasons that claims 4, 5, 15, 17, and 18 are not obvious. In addition, with respect to claim 16, the cited references fail to teach or disclose *a system wherein each of the pressure-control assembly includes . . . a pump operable to establish an increased pressure within each of said lumens, said increased pressure effective to displace any beads retained in the cavities*, as recited in claim 16. For this additional reason, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

3. The rejection of claim 10 under 35 U.S.C. § 103(a) as allegedly being obvious over Eck in view of Sakai and further in view of Ekenberg is improper

The rejection of claim 10 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view of the Sakai patent and U.S. Patent No. 4,937,048 (the “Ekenberg patent”) is improper for all of the reasons that claim 7 is not obvious because claim 10 depends from claim 7. In addition, with respect to claim 10, the cited references do not disclose or teach a system wherein *“said support is held by a frame that is (i) adapted to pivot about a substantially vertical axis, rendering movable said projection array along a substantially arcuate or circular pathway; and (ii) adapted for reciprocal linear motion along a substantially vertical pathway; such movement permitting said projections to be aligned with said ampule array and lowered so that each projection can enter a respective one of said ampules,”* as recited in claim 10.

The Eck and Sakai patents are described in detail above. As admitted by the Examiner in the Office Action, the Eck and Sakai do not disclose or teach a support that is held by a frame that is adapted to pivot about a vertical axis, rendering movable the projection array along a generally arcuate or circular pathway, and adapted for reciprocal linear motion along a generally vertical pathway.

The Ekenberg patent does not cure the deficiencies of the Eck and Sakai patents. The Ekenberg patent discloses a multi-sample magnetic separation device 20. As described in the Ekenberg patent, the apparatus and method provide for separating magnetically responsive particles from a nonmagnetic test medium in which the magnetically responsive particles are suspended. The separator 20 comprises a container 24 (e.g., a plurality of multi-well chambers) which hold the nonmagnetic test medium, one or more pins 28 disposed substantially within the test medium, an element or pin plate 30 for holding the containers, and an external magnet 34 for producing a magnetic field within the test medium. The external magnet is proximate the pins so as to create magnetic flux lines, magnetizing the pins and creating a magnetic field substantially parallel to the longitudinal axis of the pins thereof in the test medium. The container holding the test medium is positioned in the separator, producing a magnetic field operative to cause the magnetically responsive particles to be attracted to and adhere to the pins and which is substantially parallel thereto. The nonmagnetic test medium is separated from the magnetized particles, which may conveniently be washed while adhered to the pins, and subjected to further analysis,

preferably while on the pins. The apparatus is useful in separating various target substances from test media by means of substances coated on the magnetic particles which bind specifically to the target substance.

The Ekenberg patent discloses a pin plate 30 that supports the pins 28 in a fixed position and also serves as a cover for the open tops of containers 24. (See column 8, lines 66-67). As shown in FIGS. 2 and 7, end 54 of pin plate 30 is hingedly attached to base 32. End 64 of base 32 has two hinges 74a and 74b, disposed on opposite sides of end 64 for plate 30. End 54 of plate 30 has a pair of opposing pins or rods 82a and 82b extending from each side of plate 30. Channels 80 of base 32 receive rods 82a and 82b of plate 30 completing the hinges 74a and 74b. (See column 9, lines 8-31). In operation, the magnetic pack 34 is placed on top of pin plate 30 and one end 44 of the pins 28 are immersed in the test medium 26 by rotating pin plate 30 about a horizontal axis of hinges 74a and 74b.

Contrary to the assertion by the Examiner in the Office Action, the Ekenberg patent does not disclose or teach a system wherein *“said support is held by a frame that is (i) adapted to pivot about a substantially vertical axis, rendering movable said projection array along a substantially arcuate or circular pathway; and (ii) adapted for reciprocal linear motion along a substantially vertical pathway; such movement permitting said projections to be aligned with said ampule array and lowered so that each projection can enter a respective one of said ampules,”* as recited in claim 10. Accordingly, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

4. The rejection of claims 19, 20, and 48-50 under 35 U.S.C. § 103(a) as allegedly being obvious over Eck in view of Sakai and further in view of Hassler is improper

The rejection of claims 19, 20, and 48-50 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view of the Sakai patent and PCT Publication WO 97/38318 (the “Hassler publication”) is improper because the cited references do not disclose all of the features recited in the claims. As discussed above, the combination of the Eck and Sakai patents do not disclose features recited in the rejected claims, including, *inter alia*, a cavity formed with an upper ceiling region and a sidewall. The Hassler reference does not cure the deficiencies of the Eck and Sakai patents. The Hassler reference is directed to a device that counts particles received in a capillary 2 (Hassler abstract). Significantly, as shown in FIG. 1

and understood from the operation of the Hassler device, the capillary 2 does not have an upper ceiling region. Accordingly, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

5. The rejection of claims 21-25, 55, and 57-59 under 35 U.S.C. § 103(a) as allegedly being obvious over Eck in view of Sakai and further in view of Kambara is improper

The rejection of claims 21-25, 55, and 57-59 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view the Sakai patent and U.S. Patent No. 6,288,220 (the "Kambara patent") is improper because the cited references do not disclose all of the features recited in the claims. As discussed above, the combination of the Eck and Sakai patents do not disclose features recited in the rejected claims, including, *inter alia*, a system for picking up and transferring a plurality of beads and a cavity formed with an upper ceiling region and a sidewall. The Kambara patent is directed to capillaries packed with particles having various probes (Kambara abstract and FIG. 1). The Kambara patent does not cure the deficiencies of the Eck and Sakai patents because it does not disclose a system for picking up and transferring a plurality of beads and a cavity formed with an upper ceiling region and a sidewall. Accordingly, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

6. The rejection of claims 21-24, 51, 54, and 57-59 under 35 U.S.C. § 103(a) as allegedly being obvious over Eck in view of Sakai and further in view of Carre is improper

A. Claims 21-24, 51, and 57-59

The rejection of claims 21-24, 51, and 57-59 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view of the Sakai patent and European Publication EP 955084 (the "Carre publication") is improper because the cited references do not disclose all of the features recited in the claims. As discussed above, the combination of the Eck and Sakai patents do not disclose features recited in the rejected claims, including, *inter alia*, a system for picking up and transferring a plurality of beads and a cavity formed with an upper ceiling region and a sidewall. The Carre publication is directed to an apparatus for depositing high density arrays onto a support (Carre abstract and FIG. 12). The Carre publication does not cure the deficiencies of the Eck and Sakai patents because it does not disclose a system

for picking up and transferring a plurality of beads and a cavity formed with an upper ceiling region and a sidewall. Accordingly, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

B. Claim 54

The rejection of claim 54 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view of the Sakai patent and the Carre publication is improper for all of the reasons that claim 21 is not obvious because claim 54 depends from claim 21. In addition, with respect to claim 54, the cited references do not disclose or teach *a pair of spaced apart indexing holes, each being aligned with a respective indexing pin depending from a lower side of said conduit array*, as recited in claim 54. For this additional reason, withdrawal of the rejection of claim 54 is requested.

7. The rejection of claims 21 and 52 under 35 U.S.C. § 103(a) as allegedly being obvious over Eck in view of Sakai and further in view of Gilford is improper

The rejection of claims 21 and 52 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view of the Sakai patent and U.S. Patent No. 4,236,825 (the “Gilford patent”) is improper because the cited references do not disclose all of the features recited in the claims. As discussed above, the combination of the Eck and Sakai patents do not disclose features recited in the rejected claims, including, *inter alia*, a system for picking up and transferring a plurality of beads and a cavity formed with an upper ceiling region and a sidewall. The Gilford patent is directed to an apparatus for measuring light absorbance for an multiple fluid samples (Gilford abstract). The Gilford patent does not cure the deficiencies of the Eck and Sakai patents because it does not disclose a system for picking up and transferring a plurality of beads and a cavity formed with an upper ceiling region and a sidewall. Accordingly, withdrawal of this rejection under 35 U.S.C. § 103(a) is requested.

8. The rejection of claims 60-62 under 35 U.S.C. § 103(a) as allegedly being obvious over Eck in view of Sakai and further in view of Gorlich is improper

The rejection of claims 60-62 under 35 U.S.C. § 103(a) as allegedly being obvious over the Eck patent in view of the Sakai patent and U.S. Patent No. 5,447,736 (the “Gorlich patent”) is improper because the cited references do not disclose all of the features recited in

the claims. As discussed above, the combination of the Eck and Sakai patents do not disclose features recited in the rejected claims, including, *inter alia*, a system for picking up and transferring a plurality of beads and a cavity formed with an upper ceiling region and a sidewall. The Gorlich patent is directed to a method for packaging food product. The Gorlich patent does not cure the deficiencies of the Eck and Sakai patents because it does not disclose a system for picking up and transferring a plurality of beads and a cavity formed with an upper ceiling region and a sidewall.

Further, the Gorlich patent does not teach or suggest the invention of claims 60-62 for the following additional reasons. The Gorlich patent discloses a method of packaging a food product that employs a tray having side walls defining a cavity in an outwardly directed flange extending around the perimeter of the tray, the flange being adapted to receive a pair of membranes to enclose the tray. As shown and described by the Gorlich patent, each membrane 14, 16 is unwound from a pair of rolls 30, 32 and 36, 38, respectively. Accordingly, as taught by the Gorlich patent there is no take-up position.

In contrast, the invention of the present application claims a covering system for covering said beads after said beads have been disposed at said desired locations on a substrate, wherein said desired locations comprise an array of wells formed in said substrate. The covering system comprises *a continuous web of a cover material mounted for movement from a supply position to a take-up position; a shearing blade mounted for reciprocal linear motion along a direction substantially normal to said web for cutting a portion of said cover material at a region between said supply position and said take-up position*, as recited in claim 60. Therefore, it is submitted that claim 60 is not obvious in view of the cited prior art (nor are claims 61 and 62 which depend from claim 60). Accordingly, withdrawal of the rejection of claims 60-62 is requested.

IX. Conclusion

For the foregoing reasons, Applicants request that this patent application be remanded to the Patent Office with an instruction to both withdraw the outstanding rejections and allow the appealed claims.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Daniel D. Biesterveld", written over a horizontal line.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Charles Vann et al.

Confirmation No.: 6464

Serial No.: 09/506,870

Group Art Unit: 1743

Filing Date: February 15, 2000

Examiner: Bex, Patricia K.

For: **BEAD DISPENSING SYSTEM**

APPENDIX A TO APPELLANTS' BRIEF

1. A system for picking up a plurality of submillimeter beads from a bead supply and transferring said beads to a desired location, comprising:

a plurality of projections depending from a support at spaced-apart locations defining an array;

a cavity formed at a lower end region of each of said projections, each of said cavities defined by (i) a lower opening, (ii) an upper ceiling region, and (iii) a sidewall extending between said lower opening and said upper ceiling region;

wherein said upper ceiling region defines a surface extending inwardly from said sidewall; and

an attraction source, operable at said projection end regions, effective to draw beads from said supply into said cavities and to releasably retain said beads therein.

2. The system of claim 1, wherein at least a lower portion of said sidewall of each projection comprises a resiliently flexible material, such that said flexible lower portion of said sidewall can bend while maintaining the shape of said cavity so that said lower opening can bend to face said beads in said bead supply.

3. The system of claim 1, wherein each cavity has a substantially constant diameter along a region extending between its lower opening and its upper ceiling region, such that lines extending longitudinally along confronting inner surfaces of each sidewall are substantially parallel to one another.

4. The system of claim 1, wherein the diameter of said lower opening is between about 100-1,250 micrometers and the longitudinal length of said sidewall, from said lower opening and to said upper ceiling, is between about 0.50-1.25 times the diameter of said lower opening.
5. The system of claim 1, wherein the diameter of said lower opening is between about 250-750 micrometers and the longitudinal length of said sidewall, from said lower opening and to said upper ceiling, is between about 0.75-1.10 times the diameter of said lower opening.
6. The system of claim 1, wherein said cavity is dimensioned to receive at least half of one submillimeter bead, and to preclude entry therein of a substantial portion of a second such bead.
- ✓ 7. The system of claim 1, further comprising
a plurality of ampules for containing said bead supply, said ampules disposed in an array alignable with said projection array.
- 8. The system of claim 7, further comprising
a plurality of covers, each cover configured to extend over an upper opening of one of said ampules.
- 9. The system of claim 8, wherein each of said covers is a frangible membrane.
- 10. The system of claim 7, wherein said support is held by a frame that is
(i) adapted to pivot about a generally vertical axis, rendering movable said projection array along a generally arcuate or circular pathway, and
(ii) adapted for reciprocal linear motion along a generally vertical pathway;
such movement permitting said projections to be aligned with said ampule array and lowered so that each projection can enter a respective one of said ampules.

11. The system of claim 7, wherein one of said ampules holds a plurality of submillimeter beads that carry a first set of analyte-specific reagents, and another of said ampules holds a ✓ plurality of submillimeter beads that carry a second set of analyte-specific reagents; said first and second reagent sets differing from each other by at least one analyte-specific component.
12. The system of claim 2, wherein said resiliently flexible sidewall has a generally cylindrical shape, with both an inner diameter and a longitudinal depth of between about 100-1,250 micrometers.
13. The system of claim 12, wherein said inner diameter and longitudinal depth are between about 350-425 micrometers.
14. The system of claim 1, wherein said cavity is formed by a resiliently flexible, tubular sleeve fit over the end of a respective projection, said sleeve having an overhang region extending below a terminal end of said projection defining said sidewall; and wherein said terminal end of said projection, facing said cavity, defines said upper ceiling region of said cavity.
- ✓ 15. The system of claim 1, wherein each of said projections is a capillary tube having an axial lumen extending therethrough, each lumen having (i) a first end that opens into a respective one of said cavities through said ceiling region, and (ii) a second end disposed in fluid communication with a pressure-control assembly.
- ⓪ 16. The system of claim 15, wherein said pressure-control assembly includes (i) a vacuum pump operable to establish a reduced pressure within each of said lumens, said reduced pressure defining said attraction source; and (ii) a pump operable to establish an increased pressure within each of said lumens, said increased pressure effective to displace any beads retained in said cavities.
- ✓ 17. The system of claim 15, wherein each of said lumens has an inner diameter at said first end that is smaller than the diameter of a respective cavity at a location directly adjacent said ceiling region.

- ✓ 18. The system of claim 17, wherein each of said cavities has an inner diameter at a location directly adjacent said ceiling region of greater than 275 micrometers, and each of said lumens has an inner diameter at said first end of between 100-275 micrometers.
- ✓ 19. The system of claim 1, further comprising
a detection system having a field of view extending along each of said projection end regions, and adapted to sense the presence of absence of a bead retained in said cavities.
- o 20. The system of claim 19, wherein said detection system includes a plurality of elongated light-conductive fibers, each fiber having one end that extends along one of said projections and faces said cavity, and a second end disposed in optical communication with a camera device.
21. The system of claim 1, further comprising
a conduit assembly having a plurality of conduits for separately channeling a plurality of submillimeter beads released from said cavities to desired locations on a substrate, said conduits having (i) first openings at their upper ends disposed in an array having a center-to-center pitch like that of the projection array such that the first openings are substantially alignable under the projections, and (ii) second openings at their lower ends disposed in an array having a center-to-center pitch like that of the substrate array such that the second openings are substantially aligned thereover.
- o 22. The system of claim 21, wherein said second openings are disposed in an array having a center-to-center pitch substantially smaller than that of the first-opening array.
- o 23. The system of claim 22, wherein the center-to-center pitch of the second-opening array is reduced by a factor of at least about 3, as compared to that of the first-opening array.
- ✓ 24. The system of claim 21, wherein said substrate is a micro-card having a plurality of wells disposed in an array alignable under said second-opening array.

25. The system of claim 24, further comprising
a detection system having a field of view extending into each of said conduits, and
adapted to sense the presence or absence of a bead in each well of said microcard.
48. The system of claim 19, wherein said detection system includes at least one image
capture device positioned to capture and display an image that includes the lower end region
of each of said projections to provide an indication of the presence or absence of a bead
retained in the lower end region cavity of each projection.
49. The system of claim 48, wherein said detection system includes a pair of image
capture devices.
50. The system of claim 48, wherein the captured and displayed image further provides an
indication of whether more than one bead is retained in the lower end region cavity of any
projection.
51. The system of claim 21, wherein each of said conduits is curved along a longitudinal
direction from said first opening to said second opening.
52. The system of claim 21, further comprising a parallelogram linkage assembly
supporting said conduit assembly for reciprocal arcuate movement between a raised position
and a lowered position.
53. The system of claim 52, further comprising:
(i) a carousel adapted for rotation about a central axis, said carousel (a) pivotally
supporting said parallelogram linkage assembly for movement radially about a central axis of
rotation of the carousel, and (b) having a substrate holding area adjacent to said parallelogram
linkage assembly; and
(ii) a stationary rail extending along an inner region of said carousel and having a
continuous bearing surface in mechanical communication with said parallelogram linkage
assembly, said bearing surface having (a) a region disposed a first distance from central axis
and at a first vertical height, whereat said conduit array assumes said lowered position over

said substrate holding area, and (b) a region disposed a second distance from said central axis, shorter than said first distance, and at a second vertical height, higher than said vertical height, whereat said conduit array assumes said raised position.

- o 54. The system of claim 21, wherein said substrate is provided with a pair of spaced-apart indexing holes, each being aligned with a respective indexing pin depending from a lower side of said conduit array; whereupon registering said indexing pins in said indexing holes substantially aligns said second-opening array with said well array of said substrate.
- ✓ 55. The system of claim 21, further comprising a detection system having a field of view extending into each of said conduits, and adapted to sense the presence or absence of a bead on said substrate under each of said second openings.
- o 56. The system of claim 55, wherein said detection system further comprises:
 - a radiation source adapted to illuminate said substrate at locations below each of said second openings; and
 - a plurality of elongated light-conductive fibers, each fiber having (i) one end disposed to receive light traveling up through a respective conduit, and (ii) a second end that communicates with a camera device.
- o 57. The system of claim 21, further comprising a support structure, wherein said first openings are disposed in an array along one side of said support structure, and said second openings are disposed in an array along an opposite side of said support structure, wherein said first-opening array is arranged with a center-to-center pitch larger than that of said second-opening array, and wherein a region of each conduit extending from a respective one of said second openings is of capillary size, such that a liquid placed in contact with said second-opening array can be drawn at least partially into said conduits by way of capillary action.
- o 58. The system of claim 57, wherein said capillary-size region of each conduit has an inner diameter of less than about 1mm.

59. The system of claim 57, wherein capillary-size region of each conduit has inner sidewalls that are hydrophilic.
60. The system of claim 1, further comprising a covering system for covering said beads after said beads have been disposed at said desired locations on a substrate, wherein said desired locations comprise an array of wells formed in said substrate, said covering system comprising:
- a continuous web of a cover material mounted for movement from a supply position to a take-up position;
 - a shearing blade mounted for reciprocal linear motion along a direction substantially normal to said web for cutting a portion of said cover material at a region between said supply position and said take-up position.
61. The system of claim 60, wherein said cover system further comprises:
- an idler reel for holding said cover material in said supply position;
 - a driven reel for taking up said cover material in said take-up position;
 - a movable piston for effecting said linear reciprocal motion, said movable piston having a lower face on which said movable blade is mounted; and
 - a resiliently compliant, substantially planar surface provided on said lower face along a region between said movable blade for pressing said cover material against an upper surface of said substrate.
62. The system of claim 60, wherein said cover material comprises an optically clear film.